Rates and Risks of Ovarian Cancer in Subgroups of White Women in the United States

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Objective: **To provide estimates of the age-adjusted incidence and lifetime risk of ovarian cancer in subgroups of women defined by key risk factors.**

Methods: **We combined data from seven case-control studies (1122 cases and 5359 controls) with Surveillance, Epidemiology, and End Results incidence data to estimate the incidence rate and probability of developing ovarian cancer within subgroups of women defined according to the three major known risk factors: a history of ovarian cancer in the mother or sister, years of oral contraceptive (OC) use, and number of term pregnancies.**

Results: **Among women with no family history of ovarian cancer, the risk at age 65 varied from 0.3% among those who had had three or more term pregnancies and 4 or more years of OC use, to 1.6% among nulliparous women with no OC use. Among women with a positive family history, the risk of developing ovarian cancer by age 65 was estimated as 4.4% and the lifetime risk as 9.4%. The data were too sparse to estimate the risks associated with OC use and pregnancy among women with a positive family history.**

Conclusions: **The risk of developing ovarian cancer within the total population of white women can be divided informatively into component risks within subpopulations. At birth, the estimated risk of developing ovarian cancer before age 65 for the total population is 0.8%, but the component risks vary 15-fold, from 0.3 to 4.4%. *(Obstet Gynecol 1994;84:760–4)***

Each year more than 20,000 women in the United States develop ovarian cancer, and more than 12,000 die from this disease.[1] Physicians increasingly are required to put the risks of ovarian cancer into quantitative perspective, by taking into account what is known of its etiology. One potentially valuable way to describe the risks is to estimate risks within subgroups of the population defined by their levels of risk factors. This extends the common practice of describing risk within demographic subgroups.

In this analysis, we focused on three major factors influencing the risk of developing ovarian cancer: family history, pregnancy history, and oral contraceptive (OC) use. Epidemiologic studies of ovarian cancer consistently have shown the importance of these factors. We recently combined data from 12 case-control studies of epithelial ovarian cancer conducted in the United States to clarify risk factors and to refine the available estimates of the effects.[2–6] In the combined data, each additional pregnancy appeared to reduce the risk by 13–19%. Each additional year of OC use was associated with an additional reduction in risk of 5–10%. In the seven studies that collected data on family history,[7–13] women who reported ovarian cancer in one or more sisters or in their mothers were estimated to have five times the risk of women who did not.

We combined relative risk (RR) estimates from the pooled case-control data with incidence rates from the

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Table 3. Estimated Relative Risk of Ovarian Cancer Within Subgroups of United States White Women

Family history	Term pregnancy	OC (y)	Cases	Controls	RR	95% CI	Estimated incidence*	Estimated cumulative probability	
								Age 65†	Life‡
No	≥3	≥4	38	597	1.0		5.2	0.3	0.6
		1–3	72	610	1.8	1.2–2.7	9.4	0.5	1.1
		0	223	1259	2.2	1.6–3.2	11.5	0.6	1.4
	1–2	≥4	52	543	1.5	0.95–2.3	7.8	0.4	0.9
		1–3	77	478	2.6	1.7–3.9	13.6	0.7	1.6
		0	319	1008	3.7	2.6–5.4	19.3	1.1	2.3
	0	≥4	25	177	2.2	1.3–3.9	11.5	0.6	1.4
		1–3	54	157	5.8	3.6–9.3	30.3	1.7	3.6
		0	216	482	5.5	3.7–8.0	28.7	1.6	3.4
Yes			46	48	15	8.7–25	78.3	4.4	9.4
Total			1122	5359			14.9	0.8	1.8

OC = oral contraceptive use; RR = relative risk; CI = confidence interval.
* Estimated age-adjusted incidence rate among women at each risk level (cases per 100,000 woman-years).
† Estimated lifetime probability of developing ovarian cancer before age 65.
‡ Estimated lifetime probability of ever developing ovarian cancer.

(ie, hospital versus population), parity, and gynecologic surgery, the RRs were 1.5 (95% confidence interval [CI] 0.34–6.6) and 0.78 (95% CI 0.20–3.1) for no use and 1–3 years of use, respectively, compared to a baseline of 4 or more years of use. These estimates were not statistically significantly different from the null value (1.0) or from the corresponding estimates among women with no family history. If the overall RR estimates from the group of all women are applicable to the subgroup with a positive family history, the imputed lifetime risks would be 5, 10, and 14% for long-term OC users, short-term users, and non-users, respectively.

Discussion

Among white women in the United States, the average incidence rate of ovarian cancer is low at ages under 40 and rises to a maximum of about 62 per 100,000 woman-years at age 70–74.[1] At birth, the cumulative probability of developing ovarian cancer before the 65th birthday is still less than 1%, and the probability of ever developing it is less than 2%. By comparison, the lifetime risk is about 13% for breast cancer and about 3% for uterine cancer.[1] Our analysis suggests that these overall figures can reasonably be subdivided into component risks within subpopulations defined by parity, OC use, and family history.

This analysis was restricted to invasive cancers among white women. The same risk factors apparently led to the development of ovarian cancers of low malignant potential and invasive disease, despite the clinical differences in these entities and the typically younger age at diagnosis of cancers of low malignant potential.[4] Rates among white women are about 50% greater than among black women, but the known risk factors apparently operate similarly in the two groups.[6]

Our estimates of exposure-specific incidence rates are approximate; there are several potential sources of error in the data collected and in the application of patterns in these data to the national incidence figures. Errors in the questionnaire responses could have distorted the risk estimates; for example, if controls were less aware of cases of ovarian cancer in their families, the risks associated with family history would be overestimated. The geographic areas included in this analysis are not identical to the SEER areas or to a random sample of the general United States population. In addition, the case-control data reflect patterns in the early and mid-1980s. The contributions of the various risk factors to the current national burden of ovarian cancer may be slightly different, reflecting the cumulative effect of changing rates of OC use, gynecologic surgery, and childbearing. Other characteristics have been demonstrated or suggested as ovarian cancer risk factors, but they were not used to categorize women in this analysis because they are rare, are unconfirmed, or influence risk only slightly.

It would be desirable to describe subgroups of the population with more variation in risk, but this would require either a new understanding of ovarian cancer risk factors or an enormous study. Indeed, one strength of this analysis is the large number of subjects. We divided the cases into subgroups large enough to estimate the risks with some confidence, without assuming that the effects of these factors multiplied each other or interacted in any other specific way. We could have attempted to estimate the risks in smaller subgroups by using more statistical assumptions, for instance, as in

the report of Gross and Schlesselman,[17] but at the risk of errors in those assumptions.

By our estimates, incidence levels rise from five cases per 100,000 woman-years among those who report no family history, have three or more term pregnancies, and take OCs for 4 or more years, to 78 cases per 100,000 woman-years among women reporting that a sister or mother had ovarian cancer. This corresponds to lifetime risks of 0.6 and 9.4%, respectively. For women with a positive family history, the results of this analysis can be compared to the findings of Kerlikowske et al.[18] Two differences in the analyses contribute to slight differences in the reported lifetime risk in this subgroup. We reanalyzed the individual data from all the United States studies in one pooled analysis to obtain the RR estimate,[2] whereas Kerlikowske et al estimated the effect by combining the published estimates from a slightly different group of studies, including two from outside the United States. Second, we used total lifetime probability as a basis for calculation, for the reasons described by Feuer,[14] rather than the probability of developing cancer between age 35 and the expected age at death.

Despite these differences in method and presentation, both analyses strongly support the conclusion offered by Kerlikowske et al[18] that the risks in women with one or two affected family members do not approach the 50% figure reported by Piver et al[19] for women with the familial ovarian cancer syndrome. Although one may speculate how OC use alters the risk of ovarian cancer in women with a positive family history, we believe that caution is needed. The data required on the use of OCs, especially longer-term use in patients with a family history, are very sparse, even in this pooled analysis of seven United States case-control studies totaling 1122 cases and 5359 controls.

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